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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/578,507	05/26/2000	Natarajan Ramasubramanyan	2827-4	7987
23117	7590	02/25/2004		
NIXON & VANDERHYE, PC 1100 N GLEBE ROAD 8TH FLOOR ARLINGTON, VA 22201-4714			EXAMINER QIAN, CELINE X	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/578,507

Applicant(s)

RAMASUBRAMANYAN,
NATARAJAN

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29, 41-51 and 54-64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-29, 41-51 and 54-64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 May 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-29, 41-51 and 54-64 are pending in the application.

This Office Action is in response to the Amendment filed on 10/10/03.

Response to Amendment

The rejection of claims 1, 2, 4-6 and 10-16 under 35 U.S.C. 102 (e) has been withdrawn in light of Applicant's submission of Declaration under Rule 131.

The rejection of claims 1-27, 41-47, 51 and 54-62 under 35 U.S.C. 103 (a) has been withdrawn in light of Applicant's submission of Declaration under Rule 131.

The rejection of claims 44-46 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment of the claims.

Claims 1-13, 16-29, 41-51 and 54-64 are rejected under 35 U.S.C. 112 1st paragraph (written description) for reasons discussed below.

Claims 1-29, 41-51 and 54-64 are rejected under 35 U.S.C. 112 1st paragraph (scope of enablement) for reasons discussed below.

Claims 1-29, 41-51 and 54-64 are rejected under 35 U.S.C. 112 2nd paragraph for reasons discussed below.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-13, 16-29, 41-51 and 54-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: “*specification* shall contain a written description of the invention. . .[emphasis added].” The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that “as of the filing date sought, [the inventor] was in possession of the invention.” See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in “possession” of the invention claimed by describing the invention with all of its claimed limitations “by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention.” See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

In analyzing whether the written description requirement is met, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. Claims 1-13, 16, 17-21, 24-29, 41-43, 46-51, 54-56 and 59-64 recite “hydrophobic interaction media.” This term potentially encompasses any composition that is hydrophobic. The specification only describes the purification method that utilizes hydrophobic interaction columns made with methacrylate polymer, copolymer of

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methacrylate ethylene glycol or a cross-linked agarose backbone. The specification fails to describe the structural requirement of this class of composition (hydrophobic interaction media) that is related to their use in the claimed method. As such, the structural functional relationship is missing. Thus, the specification fails to describe a representative number of species by their complete structure, nor other identifying characteristics.

Claims 17-29, 41-51 and 54-64 recite “first/second/third condition surrounding said the bound first/second/third mixture.” Such condition encompasses a number of factors including temperature, pH value, salt concentration, hydrophobicity, etc. The specification only discloses that the change of salt concentration of the elution buffer to displace the nucleic acid from the column. It is unclear whether changing other conditions would also achieve the same effect. As such, the specification fails to describe a representative number of “condition” for the separation of plasmid DNA. Therefore, the written description requirement is not met.

Claims 1-29, 41-51 and 54-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for purifying plasmid DNA from a mixture of same containing at least one host cell impurity comprising: a) forming a solution with said mixture with ammonium sulfate in the range of 2M-4M to allow selective binding of host cell impurity to the hydrophobic interaction media selected from a methacrylate polymer, methacrylate polyethylene glycol copolymer or crosslinked agarose, contacting said solution with said hydrophobic interaction media, collecting plasmid DNA from said mixture; a method of separating supercoiled plasmid DNA from a mixture of relaxed plasmid DNA and host cell impurity comprising: a) forming a solution with said mixture with 3M ammonium sulfate to

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allow binding of both plasmid DNA to the hydrophobic interaction media selected from a methacrylate polymer, methacrylate polyethylene glycol copolymer or crosslinked agarose, b) contacting the solution with said hydrophobic interaction media, wash/elute the bound DNA with 2.4M ammonium sulfate to remove relaxed plasmid DNA, c) wash/elute the bound DNA with 2.0M ammonium sulfate, d) collect the supercoiled DNA; does not reasonably provide enablement for said methods for using any type of salt at any concentration, or any type of hydrophobic interaction media. Further, the methods are not enabled when other conditions such as pH or temperature are changed for separation of the relaxed or supercoiled DNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The nature of the invention is a method of purifying plasmid DNA from a mixture comprising host cell impurity by contacting the mixture with a hydrophobic interaction media which allow selective binding of the host cell impurity to said hydrophobic interaction media, and further removing unbound DNA from said mixture. The claims are further drawn to a method of separating relaxed plasmid DNA from supercoiled DNA by contacting the mixture with a hydrophobic interaction media under condition that both DNA binds said media, and alter the condition subsequently to remove relaxed DNA and supercoiled DNA separately.

The breadth of claims is broad. Claim 1 is drawn to a purification method using any type of salt solution and any type of hydrophobic interaction media for purifying plasmid DNA. Claim 17, 41 and 54 are drawn to a purification method for separating relaxed DNA and supercoiled DNA by using any type of salt at any concentration, and any type of hydrophobic

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interaction media. These claims also encompass such purification method wherein the DNA is separated by change of any condition after binding to the hydrophobic interaction media.

The teaching of the specification. The specification teaches a method for purifying plasmid DNA from a mixture of same containing at least one host cell impurity comprising: a) forming a solution with said mixture with ammonium sulfate in the range of 2M to allow selective binding of host cell impurity to the hydrophobic interaction media selected from a methacrylate polymer, methacrylate polyethylene glycol copolymer or crosslinked agarose, contacting said solution with said hydrophobic interaction media, collecting plasmid DNA from said mixture. The specification also teaches a method of separating supercoiled plasmid DNA from a mixture of relaxed plasmid DNA and host cell impurity comprising: a) forming a solution with said mixture with 3M ammonium sulfate to allow binding of both plasmid DNA to the hydrophobic interaction media selected from a methacrylate polymer, methacrylate polyethylene glycol copolymer or crosslinked agarose, b) contacting the solution with said hydrophobic interaction media, wash/elute the bound DNA with 2.4M ammonium sulfate to remove relaxed plasmid DNA, c) wash/elute the bound DNA with 2.0M ammonium sulfated, d) collect the supercoiled DNA. The specification teach specific condition such as type of salt, concentration of the salt for DNA or endotoxin binding to the hydrophobic interaction media, concentration of salt that different type of DNA can be eluted from the column, and type of hydrophobic interaction column, for which the supercoiled plasmid DNA is separated from the endotoxin, or relaxed plasmid DNA. Each of these conditions is critical for the successful purification of the plasmid DNA.

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As discussed above, the breadth of claims encompassed a purification method wherein any type of salt, salt concentration, elution condition can be used. Thus, the breadth of the claims surpasses that is enabled by the instant specification.

The state of art at the time of filing does not teach a purification method as claimed. As discussed in the specification, current available method for separating plasmid DNA from impurities or separating supercoiled DNA from relaxed DNA relies on either ion exchange chromatography or size exclusion chromatography. These methods involve the use of organic solvents, detergents, glycols or spermidine. The claimed method differs from these method since it does not use such compositions and relies on the binding of the DNA or endotoxin to the hydrophobic interaction resin under specific salt conditions. As such, the enablement of the instant claims relies primarily on the teaching of the specification.

The teaching of the specification is limited to the specific condition discussed above. The specification does not teach a purification method that can use any salt at any concentration, or use any type of hydrophobic interaction media. The specification also fails to teach a purification method wherein the binding and elution of the DNA is based on condition other than the salt concentration. Therefore, the scope of the claims surpasses that is enabled by the instant specification. One skilled in the art would have to engage in undue experimentation to practice the method as claimed. Thus, the claimed invention is enabled to the scope indicated above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-29, 41-51 and 54-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-16, the recitation of “collecting unbound plasmid DNA from said complex” renders the claims indefinite because how the unbound plasmid DNA can be part of complex. According to the prior steps in claim 1, it is the impurity that forms a complex with the hydrophobic interaction media, and the plasmid DNA is free. Clarification is required.

Regarding claims 17-29, 41-51 and 54-64, the recitation of “remove supercoiled plasmid DNA from said second bound mixture...” renders the claims indefinite because it is unclear how the supercoiled plasmid DNA become part of the second bound mixture. According to the prior steps, the second bound mixture comprises the relaxed plasmid DNA, whereas the supercoiled plasmid DNA is not part of the second bound mixture. Clarification is required.

Regarding claim 14, the recitation of “a least one of a propyl...” renders the claim indefinite. It appears that there is a typographical error, wherein it should be “at least one of a propyl...”


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine Qian, Ph.D.


ANNE-MARIE FALK, PH.D.
PRIMARY EXAMINER